#18

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 023533/0130

Patent application of
HERMONAT *et al.*

Group Art Unit: 1636

Serial No. 09/693,908

Examiner: B. D. Chism

Filed: October 23, 2000

For: ADENO-ASSOCIATED VIRUS (AAV) REP78 MAJOR REGULATORY PROTEIN, MUTANTS THEREOF AND USES THEREOF

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents
Washington, D.C. 20231

Considered
10/03/03
BD

I, Paul L. Hermonat, hereby declare:

1. I am an inventor of the captioned application. I have worked in the field of papillomaviruses and methods of studying and recombinantly manipulating these viruses since 1985. I have published over 75 papers with a number of these papers in the papillomavirus field (see my CV), and I am an inventor of U.S. 5,139,941 and U.S. Patent No. 6,153,436. I received a Ph.D. in Medical Microbiology and Immunology in 1984 from the University of Florida, Gainesville, College of Medicine, did post-doctoral fellowships at the University of Florida, Gainesville, College of Medicine, Department of Pathology and at the National Cancer Institute, Laboratory of Tumor Virus Biology (1984-1988), and joined the Department of Obstetrics and Gynecology at the University of Arkansas for Medical Sciences in 1990. I have been invited to numerous international conferences as a speaker or participant Attached is my CV to further explain my experience and background.

2. In support of showing that the present invention is enabled for *in vivo* therapeutic uses in treating papillomavirus associated diseases or cancers, I provide a copy of a publication entitled "Adeno-Associated Virus is Associated with a Lower Risk of High-Grade Cervical Neoplasia," by Coker *et al.*, of which I am an author, which provides data based on cervical DNA analysis for AAV and HPV. This publication supports the hypothesis that AAV positive

patients had a reduced risk of squamous intraepithelial lesions (SIL). The introduction to this publication cites many scientific articles that support this relationship between AAV and HPV. Particularly, relevant to the question of enablement of the *in vivo* therapeutic use, is the last sentence on page 83, second column, where the inhibitory effects of AAV on papillomavirus transcription, replication and oncogenic transformation, have been mapped to the full-length product of the AAV *rep* gene, the Rep78 protein. The 1994b Hermonat publication and the 1995 Horer publication are already of record in the present application but additional cited publications, including the Coker publication support applicants' position that the wild-type AAV Rep78 protein is responsible for the inhibitory effects of AAV on papillomaviruses. Enclosed with this declaration are several of these publications.

3. In regard to the use of an AAV Rep78 modified protein to inhibit a papillomavirus or an oncogene, the specification of the above-identified application, beginning at page 25, line 30 to page 27, line 13 and including the results presented in Figures 10-14, shows that the AAV Rep78 mutant, AAV Rep-192^{HG} binds more strongly to specific DNAs as compared to the wild-type AAV Rep78 protein. Thus, it is a logical conclusion to a skilled person, such as myself, that if the wild-type AAV Rep78 protein inhibits papillomavirus replication as shown in my enclosed publications, then it follows that an AAV Rep78 mutant, such as AAV Rep-192^{HG}, which binds better to DNA sequences than the corresponding wild-type AAV Rep78 to the same DNA sequences, would be a stronger inhibitor of papillomavirus or oncogenes.

4. I hereby declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

By: _____ Date: 7/11/09

Paul L. Hermonat, Ph.D.